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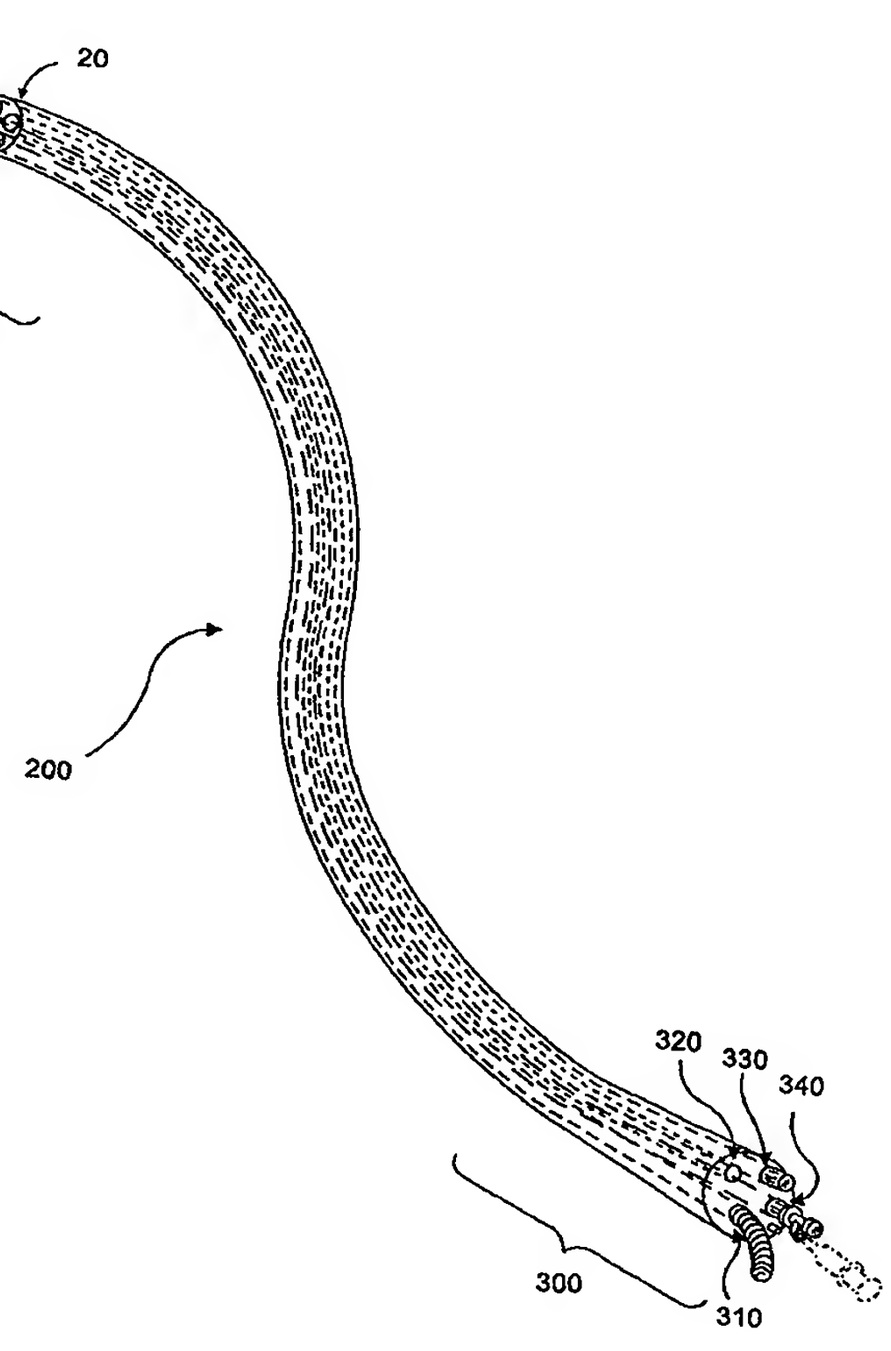
(54) Title: MEDICINAL AGENT ADMINISTRATION CATHETER DEVICE

(57) Abstract

A catheter apparatus for the intraorgan administration of medicinal agents, such as cells, genes, drugs, other agents and soluble protein factors such as growth factors into a designated site within an organ approached via entry points in the arterial or venous circulatory system, cut–down sites, surgery, introducer ports during minimally invasive surgery, or body orifices including the mouth, esophagus, trachea, urethra, and anus, etc. The device consists of a catheter device with one or more compartments housing one retractable hollow bore needle for the dispersion of medicinal agents into a target tissue, an anchoring means for stabilizing the end of the catheter to a surface, such as the endocardium, of the target organ and a guiding wire for directing the catheter to a specific location. The control means are located at the proximal end of the inventive device and located external to the patient.



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MEDICINAL AGENT ADMINISTRATION CATHETER DEVICE

FIELD OF THE INVENTION

This invention relates to a catheter device and method for the administration of a medicinal agent, such as cells, genes, drugs or other agents into a designated site within organs or tissues of the body. Particularly, this invention relates to the administration of protein growth factors and/or genetic material into the myocardium of the heart.

BACKGROUND OF THE INVENTION

Recent research has shown that cells residing within the wall of the heart synthesize, secrete and respond to a variety of soluble protein factors such as cytokines and lymphokines (Mann, Cytokine & Growth Factor Reviews 1996; 7:341-354), and the importance of these soluble protein factors is beginning to be realized by scientists and clinicians in the area of cardiovascular disease (Dzau et al, A J Cardiol 1997; 80(9A):331-391).

A partial list of these soluble protein factors includes fibroblast growth factor (Bogojevitch et al, J. Bio.Chem. 1994; 269:1110-1119), epidermal growth factor (Brown et al, New Eng. J. Med. 1989; 321:76-79), transforming growth factor-beta (Lefer et al, Science 1990; 249:61-64), platelet-derived growth factor (Hom et al, Ann Otology Rhinology Laryngology 1992; 101(4):349-354), insulin-like growth factor I (Delafontaine P., Cardiovasc. Res 1995; 30(6):825-834), vascular endothelial growth factor (Ferrara et al), angiotensin II (Dzau, J. Hypertension 1994; 12(4):S3-S10), angiotensin converting enzyme, tumor necrosis factor-alpha, interleukin-1, interleukin-2, interleukin-6, endothelin-1, cardiotrophin-1 (Pennica et al, Proc Natl. Acad. Sci. USA 1995; 92(4): 1142-1146)

and myotrophin. It is likely that additional soluble protein factors within the heart and elsewhere in the body will be identified in the future.

Within the cardiovascular system, these soluble protein factors are associated with a variety of cardiac pathologies including myocardial infarction (Cruickshank et al, Lancet 1994; 343:974), congestive heart failure (Ferrara et al, Circulation 1995; 992(6):1479-1486), acute and chronic myocarditis (Matsusmori et al, Eur. Heart J. 1991; 12:203-205), myocardial reperfusion injury (Lefer et al, Science 1990; 249:61-64), hypertrophic cardiomyopathy (Pennica et al, Proc. Natl. Acad. Sci. USA 1995; 92(4): 1142-1146), dilated cardiomyopathy (Marriott et al, Heart 1996; 75(3): 287-290), acute and chronic allograft rejection in cardiac transplantation (Sakobar et al, Clin. Transplantation 1993; 7:459-466) and cardio-pulmonary bypass (Butler et al, J. Thorac Cardiosacs. Surg. 1993; 105:25-30).

These and other soluble protein factors are ubiquitous throughout the body (Mimni, Biomaterials 1997; 18:1201-1225). Their importance in many areas is being demonstrated; for example, they play a role in angiogenesis in cancer (Folkman et al, Science 1987; 235:442-447). Emerging information suggests that these soluble protein factors are important mediators in the cardiovascular system which enable the heart to adapt to abnormal pathophysiological conditions (Mann, Cytokine & Growth Factor Reviews 1996; 7:341-354). They assist the heart in maintaining myocardial homeostasis by modulating tissue repair, neovascularization and tissue remodeling. In some cases, the changes mediated by the soluble protein factors are beneficial to the cardiovascular system. In other cases, the changes are insufficient to compensate for the pathophysiological conditions, or have become maladaptive.

Based on the preliminary scientific studies, it seems likely that some of these soluble protein factors will play an important role in clinical medicine in the future (Folkman, New Eng. J. Med. 1995; 333:1757-1763). They can be used as novel diagnostic and treatment modalities in cardiovascular diseases. Until now, these soluble protein factors, genes, cells and other agents have been used experimentally in cardiovascular diseases. In other organ systems, they have been used clinically, but only to a limited extent.

The advancement of soluble protein growth factor research and the transition from this research into clinical applications will require a new drug delivery system which is capable of delivering these soluble protein factors, genes or cells directly into a designated area within a target tissue such as the wall of the heart.

Current methods of drug and medicinal agent administration include oral, subcutaneous, intradermal, intramuscular, intravenous, intra arterial and transdermal approaches. They all share the characteristics of distributing the drugs via the circulatory system and disseminating them systemically. Soluble protein factors administered by these methods may be subject to rapid degradation before reaching the target organ or before achieving high concentration within the target tissue.

The current methods are also ineffective for the delivery of cells to some target tissues, for example, the myocardium of the heart. When using intravenous and intra arterial administration, the cells may become trapped in non-specific capillary beds which can result in the failure of a substantial number of the

cells to reach the myocardium. Furthermore, the cells may become trapped in the coronary circulation, resulting in myocardial ischemia.

The implantation of cells into the myocardium may become clinically important for at least two reasons. The implantation of cells that secrete soluble protein factors, for example cytokines and lymphokines, may supplement failing or lost production of these factors, and the transplantation of myocytes to replace dying or dead myocytes may improve cardiac function. Furthermore, cellular transplantation into other locations in the body may come into clinical use in the future.

Many, if not all, of the soluble protein factors identified thus far within the heart are present elsewhere in the body. Administration of the soluble protein factors in a non-specific fashion may result in systemic effects including undesirable side-effects and adverse reactions. Therefore, it may be necessary in some cases to administer the soluble protein factors, genes, cells or other medicinal agents to a specific site in the target organ such as the wall of the heart.

While soluble protein factors, genes and certain cells within the heart are only recently being investigated for roles in the cardiovascular system, there is already a substantial body of knowledge relating to them in the other systems of the body. Some soluble protein factors are currently available in human recombinant forms and have been used clinically for treatment of diseases. Based on these clinical experiences, these medicinal agents, in some cases, need to be administered directly to the tissue or organ which they will affect in order to maximize their medical efficacy and efficiency.

A device and method for the delivery of a medicinal agent to a target organ is disclosed in U.S. Patent application Serial No. 08/961,124, filed October 31, 1997, the contents of which are hereby incorporated herein by reference.

Patients with coronary artery disease are currently treated with a variety of anti-angina medications. There are several disadvantages associated with these medications: patients have to take them on a long-term basis and some of these medications are expensive; they are not always effective and are sometimes associated with undesirable side-effects; and many patients go on to require additional interventions for their coronary artery disease.

Patients with more severe coronary artery disease are treated either with percutaneous transluminal coronary angioplasty or coronary artery bypass grafting. While angioplasty requires a shorter hospitalization and is a less invasive procedure than bypass surgery, it is associated with a high frequency of early failure. Studies have shown that 20 to 35% of patients who undergo one angioplasty will require a second angioplasty within 18 months. Moreover, angioplasty cannot be performed in every patient.

Bypass surgery has a better long-term result but is a major operation. Accordingly, the procedure is associated with higher morbidity and mortality rates than angioplasty. The operation is painful and uncomfortable for the patient, and the length of convalescence can be considerable. Moreover, bypass surgery is an expensive procedure.

In some diseased coronary arteries, neither angioplasty nor bypass surgery can be performed because the vessels are either too small or the disease too diffuse. For this last group of patients, there is presently no treatment available.

Recently, a technique using neovascularization has been attempted for the treatment of coronary artery disease. As used herein, neovascularization is defined as the formation of a network of small vessels and is one component of the healing process afrer certain types of injury. Neovascularization is promoted by several soluble protein factors. It is known that a needle can create an injury in the myocardium which begins the process of neovascularization. This technique offers some promise for treating this disease and new and/or improved devices and methods are needed to implement its use.

SUMMARY OF THE INVENTION

We have discovered a new device and method for delivery of liquid medicinal agents directly to bodily organs. In addition, the inventive device is particulary suited for neovascularization methods and techniques.

To perform the administration of a medical agent from inside the target organ or tissue, we have developed a catheter device and method for the administration of a medicinal agent, such as soluble protein factors, genes, cells, drugs and other agents into a designated site of a target organ or tissue, such as the myocardium. This catheter device approaches the myocardium from the endocardial surface of the heart via entry points in the circulatory system, either arterial or venous. In other applications, the catheter device may be used in the abdominal or thoracic cavities or elsewhere in the body via an introducer, e.g., an endoscopic

device, as part of a minimally invasive procedure. This catheter device may also be introduced into the body via a cut-down or during any operative procedure at any location on the body. Finally, the inventive catheter may be introduced into the body via openings, such as the mouth, trachea, urethra, anus, etc.

While this catheter device is developed primarily for cardiovascular diseases, which are the primary focus of this patent, there will likely be other clinical applications, and these are included in the scope of this patent. We describe the use of the catheter device in coronary artery disease here only as one example in several possible applications in order to illustrate the potentials of the catheter device.

The inventive catheter provides a means of creating the injury from inside the heart. The inventive catheter also provides a means to augment the neovascularization process with the administration of a specific soluble protein factor or gene that codes for the soluble protein factor into the injury site. This combination of methods, injury plus provision of soluble protein factors, may stimulate the formation of neovascularization to a greater extent than either method alone. The neovascularization will increase the supply of oxygenated blood to the ischemic myocardium in a manner similar to collateral circulation.

For the treatment of coronary artery disease, the catheter device will be used to create injury and to administer a soluble protein factor or a gene coding for the factor in two seemingly similar approaches but with different biological basis.

In the first approach, The area "treated" will be the territory of the ischemic myocardium supplied by the diseased coronary artery. In this area, the needle in the catheter device will repeatedly "seed" the ischemic myocardium with small needle tracks. Each needle track will extend from the left ventricular chamber through partial thickness of the myocardium and provide an angiogenesis factor. The rationale behind this maneuver is that injury supplemented by an angiogenesis factor will augment neovascularization. The collateral circulation resulting from neovascularization will bring oxygenated blood from the left ventricular chamber into the ischemic myocardium.

In the second approach, the "treated" area will be the myocardium immediately adjacent to each stenosis in the coronary arteries. The needle in the catheter device will create a few small needle tracks and administer an angiogenesis factor or genes that code for the factor. The rationale behind this maneuver is to augment the coronary artery to coronary artery collateral circulation that is already present at the time of the procedure.

Depending on the clinical situation, either or both approaches may be used in each patient being treated for coronary artery disease.

Accordingly, it is an object of the present invention to provide a minimally invasive delivery system for medicinal agents, including cells, genes, drugs such as soluble protein growth factors and other therapeutic agents, which can administer the medicinal agents in high concentration to a specific site in a target organ or tissue of the body.

It is a further object to provide a minimally invasive delivery system for medicinal agents, including cells, genes, drugs such as soluble protein growth factors and other therapeutic agents, which can administer the medicinal agents in high concentration to a specific site in the heart, particularly the wall of the heart.

It is another object of the present invention to provide a minimally invasive delivery system which can specifically and efficiently distribute a medicinal agent, including cells, genes, drugs such as soluble protein growth factors and other therapeutic agents, onto an extended area of the heart or other target organ or tissue.

It is yet another object of the present invention to provide a delivery system that can approach a target organ or tissue from the arterial or venous circulatory system via one or more of the following routes: an introducer during minimally invasive surgery, a cut-down site, a "traditional" operation and from body orifices such as the mouth, esophagus, trachea, urethra, anus, etc.

It is a further object of the present invention to provide an injection system which can be anchored to a surface of a target organ or tissue, so that the organ can be controllably and reliably injected, even if the organ, such as a beating heart, is in motion.

Specifically, we have discovered that the above and other objects of the invention may be achieved by a device for administering a medical agent directly to a bodily organ comprising a hollow catheter having a proximal end and a distal end; anchoring means for securing the distal end of the catheter to an organ surface, the anchoring means being movable between a retracted position in which the anchoring means is within the catheter and an attachment position in which at

least a portion of the anchoring means protrudes from the distal end of the catheter for securement to an organ surface; anchor control means for moving the anchoring means between the retracted position and the attachment position; and medical agent delivery means within the catheter for delivering a medical agent to a bodily organ.

Further objects and advantages of the present invention will become apparent from a consideration of the drawings and the following descriptions.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a perspective schematic view of a catheter device in accordance with the invention;

Figure 2 is a partial perspective, exploded cross-sectional view of the catheter device of the invention showing a guiding wire within one conduit;

Figure 3 is a schematic, perspective, partial view showing the distal opening and closing means to the conduit housing the guiding wire at the distal end of the catheter device according to the present invention;

Figure 4 is a schematic, perspective, partial view showing a guiding wire protruding from the closing means at the distal end of the catheter device according to the present invention;

Figure 5 is a partial cross-section of the distal end of the catheter device showing the hypodermic needle in the conduit of the catheter device according to the present invention;

Figure 6 is a schematic, perspective, partial view of the distal end of the catheter device according to the present invention showing the conduit enclosing an anchoring means of a helical coil with a sharpened tip in a retracted position;

Figure 7 is a schematic, perspective, partial view of the distal end of the catheter device according to the present invention showing the anchoring means extending or protruding from the opening of a conduit;

Figure 8 is a partial cross-section of the distal end of the catheter device according to the present invention showing a mechanism for the anchoring means with said means in an extended position;

Figure 9 is a cross-section of the catheter device at the mid-section showing the actual distance relationship between the different conduits according to the present invention;

Figure 10 is a partial perspective view of the catheter device showing a variation of the proximal end of the catheter according to the present invention;

Figure 11 is a cross-sectional detail of the catheter device according to the present invention showing the control mechanisms at the proximal end of the catheter device for the advancement and retraction of the hypodermic needle, injection of the medicinal agent and prevention of foreign bodies or fluid from entering the needle or injection control means;

Figure 12 is a schematic, perspective, partial view of the catheter device according to the present invention showing a guiding wire protruding from its conduit at the proximal end of the catheter device;

Figure 13 is a schematic, perspective, partial view of the catheter device according to the present invention showing the needle and injection control mechanisms at the proximal end of the catheter device;

Figure 14 is a cross-sectional detail of the catheter device according to the present invention showing a control mechanism at the proximal end of the catheter device for the engagement and disengagement of the anchoring means according to the present invention;

Figure 15 is a cross-sectional detail of the distal end of an alternative embodiment of the catheter device which combines the functions of the needle and anchoring means into a single unit;

Figure 16 is a cross-sectional detail of the proximal end of the catheter device of Figure 15.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the present invention is a catheter device for delivering a medicinal agent to a specific site within a target organ or tissue.

Specifically, the invention is a hollow catheter having a distal end, a proximal end having one or more continuous conduits, sometimes referred to in the art as lumens, from the distal end to the proximal end. The distal end is placed against the target site, usually within the target organ, while the proximal end of the catheter device remains external to the patient and under control of the operator.

The conduits contain, at the distal end of the catheter, a hollow bore needle which is used to penetrate the myocardium or other target tissue and which is used to disperse the medicinal agent into the designated site and a means for anchoring or attaching the tip of the catheter device to the endocardial surface or the lining surface of another target organ. The conduits may additionally contain, at the distal end of the catheter, a means for guiding the distal end of the catheter device to a designated site on the endocardial surface of the left ventricular chamber or other target location. At the proximal end of the catheter are located the means for controlling the guidance, anchoring and injecting functions of the catheter.

The hollow bore needle has one entrance opening and one to a plurality of exit openings. The entrance opening of the needle is in communication with tubing which runs the length of the same conduit the needle resides in for the conveyance of a medicinal agent from the proximal end of the catheter to and through the hollow bore needle. The one to several exit openings on the hypodermic needle are for the administration of the medicinal agent into the wall of the heart or another target tissue. The needle is capable of being retracted entirely within the distal end of the catheter device. It is movable to allow a sufficient portion of the needle to protrude from the distal end of the catheter device in order to penetrate for a measured depth into the wall of the heart or other target tissue. The means for retracting and moving the needle at increments are at the proximal end of the catheter device, external to the patient and under the control of the operator.

The distal end also includes an anchoring means for anchoring or attaching the distal end of the catheter to the endocardial surface in the heart chamber or the surface of another target organ. Embodiments of the anchoring means include, but are not limited to, a spring-like means of a helical coil with a

pointed tip or a prong-like means with a plurality of pointed tips. The anchoring means is capable of being hidden within the distal end of the catheter device when fully retracted. This anchoring means is movable to allow a sufficient portion of the mechanism to protrude from the distal end of the catheter device such that the tip of the catheter device may be anchored or attached to the endocardial surface of the heart or other target site. The anchoring or attachment is accomplished with the helical coil by a screw-in mechanism. In the case of a prong-like means of anchoring, for example, a three-prong grasping mechanism accomplishes the attachment. From the proximal end of the catheter device, the operator is capable of manipulating the distal end of the catheter device in anchoring or attaching and in detaching the distal end to the endocardial surface or other target sites. Once the distal end of the catheter device is anchored or attached to the endocardial surface or other target sites, the operator advances the needle which has, until now, been retracted within a conduit in the catheter device. The needle then enters the myocardium or other target tissue, depending on the clinical application.

The very distal end of the catheter device may be manufactured of a semi-rigid material. This provides the rigidity necessary to advance the needle into the myocardium or other target tissue and to protect the retracted needles and anchoring devices. The distal end of the catheter may also contain closing means covering the distal openings of the conduits to prevent entry of matter into the conduits, while allowing emergence of the needle or anchoring means contained in the conduit.

The needle is in communication with tubing which runs through a conduit of the catheter device and connects to a syringe or reservoir external to the patient for the administration of a medicinal agent.

A guiding wire can be inserted within a separate conduit or compartment within the catheter device. This guiding wire runs within about the entire length of the catheter device. It is removable and exchangeable by the operator and is available in different rigidity, angulations and curvatures to facilitate placement and attachment of the catheter device in the left ventricular chamber or other target locations and for localization of the catheter device tip to a specific site on the endocardial surface or elsewhere. In another configuration of the guiding wire, the distal end of the guiding wire may flex and extend forward and backward, to the right and to the left, and to in-between positions . These movements of the distal end of the guiding wire are controlled by the operator. The guiding wire also facilitates placement of the distal end of the catheter device to other target sites depending on the clinical situation. In some embodiments of the inventive catheter, the guiding wire may be omitted.

The catheter device is manufactured of a disposable or a reusable material, which may be radio-opaque during fluoroscopy for monitoring the position of the catheter in the patient. There may be markings on the external aspect of the catheter device to indicate length measurements.

The controls for operating the catheter device are external to the patient and include means for advancing and retracting the hollow bore needle in measured increments; means for advancing and retracting, anchoring and detaching the means which anchors the tip of the catheter device to the endocardial surface or another surface; means for inserting and removing the guiding wire within the catheter device; means for manipulating the movement of the distal end of the guiding wire; and means for administering a medicinal agent in measured amount from a syringe

or reservoir through the conduit within the catheter device into the needle and out the needle exit opening(s) into the wall of the heart or other target tissue.

The inventive catheter may be introduced into the body using several approaches. The primary approach is from an entry point, such as the femoral artery or the femoral vein, in the arterial or the venous circulation. For example, the inventive catheter may be introduced in a retrograde fashion into the left ventricular chamber via the femoral artery and aorta to deliver a medicinal agent to the wall of the heart. Another approach is via an introducer as part of a minimally invasive procedure in the abdomen, chest or elsewhere in the body. The inventive catheter may also be introduced into the body from a cut-down site anywhere in the body or during an operation of any kind. Finally, the inventive catheter may be introduced into the body from orifices such as the mouth, esophagus, trachea, urethra, anus, etc. By these various methods, the present invention may be used for the delivery of a medicinal agent to a wide variety of target sites, including the pulmonary circulation, the coronary circulation, the urinary bladder, etc.

The medicinal agents which the catheter is capable of delivering to a target site include cells, genes, soluble protein factors such as growth factors, other drugs and other agents.

Many embodiments of the inventive device are possible. The following description is one of the preferred embodiments. The inventive apparatus may be configured in a range of sizes, diameters, and lengths depending on the clinical application. It is made of disposable or reusable materials. The catheter may be made of radio-opaque materials so that it can be detected by fluoroscopy.

Figure 1 depicts an embodiment of the catheter device. Additional components may be added or existing components deleted, depending on the clinical requirements. As shown, the inventive device comprises a proximal end 300 and a distal end 100 in the configuration of a catheter device 200 comprising four conduits, each of which is continuous from the distal end to the proximal end. Control means are at the proximal end 300 of the catheter device. The proximal entry to conduit 310 is intended for the introduction, manipulation and removal of a guiding wire. Conduit 320 is unoccupied and is intended for some future applications that may arise. The proximal entry of conduit 330 houses the means that controls an anchoring or attachment mechanism at the distal end of the catheter. The proximal entry of conduit 340 houses the means for controlling the hypodermic needle and the transferring of a medicinal agent to the needle at the distal end of the catheter device as well as means for preventing the entry of foreign bodies or fluid into the needie control means or the means of transferring the medicinal agent. One or more of the conduits within the catheter may be deleted depending on the clinical application.

The distal end 100 is available in different sizes and shapes as well as other specifications depending on the clinical requirements. Similarly, the proximal end 300 is available in different sizes and shapes and other specifications depending on the clinical requirements.

The distal end 100 of the inventive device contains four exits for the four conduits of the catheter. Each exit may be provided with a closing means to prevent the entry of foreign bodies or fluid into the conduit. Distal exit 10 is in continuity with conduit 310, which contains the guiding wire. Exit opening 20 is unoccupied and may be used for some future clinical applications. Exit opening 20

communicating conduit 320 may be absent in some configurations (not shown) of the inventive apparatus. Exit opening 30 is in continuity with conduit 330, which contains the anchoring or attachment mechanism. Exit opening 40 is in continuity with conduit 340, which contains the hypodermic needle and conduit tubing.

In order to direct the distal end of the catheter device to the specific site of injection in the body, the operator uses a set of guiding wires of differing rigidities, angulations and curvatures which are sized to fit within the conduit 310 of the catheter device.

Figure 2 depicts a curved guiding wire 15 within its lumen or conduit 310 and the distal exit opening 10 at the distal end 100 of the catheter. The guiding wire may be exchanged for a differently shaped wire and manipulated by the operator during each procedure.

In order to prevent entry of foreign objects into the distal openings of the conduits or the blockage of the conduits, the conduits may be equipped with closing means over the openings. Figure 3 depicts the closing means 12 of exit 10 containing a guide wire 15 in a retracted or hidden position at the distal end 100 of the catheter device. Closing means 12 is a cover formed of an elastic deformable material having a hole in it small enough to prevent the entry of body fluids into the conduit during use of the catheter. The material sufficiently deformable to allow the hole to stretch to allow the exit of the tip of the guide wire when the guide wire is pressed against the closing means. The material is sufficiently elastic to allow the hole to return to a body fluid-excluding size when the guiding wire is subsequently retracted.

Figure 4 depicts the same opening 10 as Figure 3, after the tip of the guide wire 15 has emerged from exit opening 10 at the distal end 100 of the catheter device.

Figure 5 depicts in cross-section a hypodermic needle 45 emerging from distal exit opening 40. The hypodermic needle 45 is connected to a conduit tubing 46, both being housed in the conduit 340 and wall of same 47. The hypodermic needle may have other configurations (not shown) with variations in the number of exit openings, angulations, and curvatures. For Example, the hypodermic needle may have no exit openings at the distal end but exit opening(s) on the side-wall of the needle.

In order to better manipulate the needle into the tissue at the specific site, it is desirable to anchor or attach the distal end to the surface of the specific site. Figures 6, 7 and 8 depict one embodiment of the anchoring means for use with the catheter device according to the present invention. Figure 6 depicts the exit opening 30 of conduit 330 containing the spring-like, helical coil mechanism 38 in a retracted, hidden position at the distal end 100 of the catheter device. Figure 7 depicts the spring-like, helical coil mechanism 38 in the anchoring position, emerging from the exit opening 30 at the distal end 100 of the catheter device. By use of the anchoring control means, the spring-like mechanism can be twisted between the retracted position and the anchoring position. When the distal end of the catheter device is against a tissue, the twisting of the spring-like means as it is moved from the retracted position to the anchoring position causes the sharpened tip 36 and one or more turns of the spring-like mechanism to enter the tissue, thereby attaching the distal end of the catheter device to the tissue. Although Figure 7

depicts approximately two turns of the helical coil emerging from exit opening 30, fewer turns will be sufficient in some cases for anchoring the catheter to the tissue.

Figure 8 is a partial cross-sectional view of Figure 7 along section line 8 and depicts the means by which the spring-like mechanism of Figure 6 and 7 is moved between the retracted position and the anchoring position. The means comprises a helical coil 38 which is connected to the end of a rod 34 that abuts the wall 31 of the conduit containing the spring-like mechanism near the distal opening 30. This rod 34 continues within the conduit of the catheter and emerges at the proximal end (not shown) of the catheter. The distal end of the wall 31 is lined with threads 32. Helical coil 38 is comprised of helical turns 33. The helical turns 33 and threads 32 on the wall of the lumen or compartment are engaged such that when the operator turns the rod 34 at the proximal end of the catheter device, rod 34 with the helical coil 38 either advances forward or backward relative to the catheter device.

Figure 8 also depicts a closing means for preventing foreign objects or fluid from entering the conduit. Gaskets 35 between rod 34 and wall 31 prevent the passage of foreign objects or fluid through the space between the rod and the wall toward the proximal end of the conduit. Similar gaskets may be used as closing means in other conduits of the catheter, for example, gaskets may be placed between the tubing communicating with the needle and the wall of the conduit containing the needle.

As an alternative to the spring-like anchoring means shown in Figures 6-8, an anchoring means comprising three or more prongs may be used to pierce or grasp the surface of the specific site on the desired organ or tissue.

The previous figures have all depicted the size of the lumens and their spacing relative to the size of the catheter schematically for easier understanding. Figure 9 provides a true representation of the relative size and spacing of the lumens in the catheter device. Essentially, they are packed as tightly as possible into the catheter in order to minimize the cross-sectional size of the catheter.

Figure 10 depicts an alternative embodiment of the proximal end 300, which remains external to the patient and houses the control means (not shown in this figure) for the catheter device. In this embodiment, the proximal end 300 is of a greater diameter than the rest of the catheter to increase the surface area of the working platform, thereby making manipulation of the controls easier.

Figure 11 depicts an embodiment of the needle control means, the injection control means and a means of preventing entry of foreign bodies or fluid into the needle or injection control means. The needle control means comprises the tube 46 which is in communication with the needle (not shown), needle depth control 41, and spring 42 which biases tube 46 away from the needle depth control 41, thereby retaining the needle inside the distal end of the catheter. The operator advances the needle by pressing tube 46 through the conduit 340, compressing spring 42, until shoulder 43 of tube 46 comes into contact with shoulder 44 of needle depth control 41. The distance the of needle advances outside the catheter is determined by the distance between the shoulders 43 and 44. By twisting the needle depth control 41, which is threaded to match threads in the proximal end of conduit 340, the distance between the shoulder 43 of the tube and the shoulder 44 of the needle depth control can be adjusted as required by the operator. A set of markings (not shown) on the outside of needle depth control 41 or other measurement markings may be used to indicate the distance of needle travel allowed by any

particular placement of the needle depth control. When the operator releases tube 46, then spring 42 will cause the needle to retract into the distal end of the catheter. Spur 48 is attached to tube 46 and is fitted into slot 49 in wall 47 of conduit 340. Spur 48, in combination with slot 49, prevents spring 42 from retracting the needle farther into the catheter than the retracted position. Spur 48, in combination with slot 49, also prevents the twisting of the needle depth control from also twisting tube 46 in the conduit.

The injection control means depicted in Figure 11 is syringe 50, which is in communication with tube 46, and therefore also with the needle.

The means of preventing entry of foreign bodies or fluid into the needle or injection control means in the embodiment of Figure 11 comprises gaskets 60 and conduit 62 which intersects conduit 340 as a point distal to the gaskets 60. Gaskets 60 provide a fluid-tight fit between the tube 46 and the wall 47 of conduit 340 and prevent any foreign bodies or fluid from passing from the distal side of the gaskets to the proximal side. Conduit 62 has a proximal opening 64 through which a fluid such as sterile saline can be applied under positive pressure to provide a constant wash through the portion of conduit 340 distal to the gaskets 60, preventing the blockage of the conduit with blood and allowing the purging of air from the conduit.

Figure 12 depicts a guiding wire 15 emerging from the entrance 310 at the proximal end 300 of the invention apparatus. As described earlier, this guiding wire 15 comes in different rigidity, angulations, and curvatures. The operator can freely interchange the guiding wire 15 during each procedure in order to guide the tip of the catheter device 100 to a designated site inside the heart

chamber or another location in the body. This is performed under fluoroscopic control, when indicated, and may or may not be assisted by other monitoring equipments.

Figure 13 depicts in a perspective view the placement of the needle control means and injection control means at the proximal end of the catheter.

Figure 14 details an embodiment of the control means for the spring-like mechanism of Figure 8. It comprises rod 34 which is in continuity with the distal end of same containing the anchoring mechanism. The handle 335 of rod 34 abuts the wall 330 of the conduit or lumen. By turning the handle either in a clockwise or in a counter-clockwise direction, the screw-in mechanism either retracts backward into the lumen or extends forward from the lumen, engaging the endocardial surface or other tissue surface. A set of markings (not shown) on the outside of rod 34 may be used to indicate the correlation between the turning of the rod and the vertical distance traveled by the spring-like mechanism.

Figures 15 and 16 depict an additional embodiment in which the needle and the anchoring means are combined. A hollow helical coil needle 70 is attached to rod 72 and in communication with passage 74 in rod 72 at the distal end of the catheter, as shown in Figure 15. Rod 72 and passage 74 extend the length of the catheter to emerge at the proximal end of the catheter, as shown in Figure 16, where passage 74 is in communication with an injection control means such as tube 76 and syringe 78. The helical needle is advanced or retracted by twisting handle 372 to rod 34, in an identical manner as the helical coil was advanced or retracted. Once the needle is inserted into the target tissue, thereby anchoring the distal end of the catheter to the tissue, the injection control means can be used to inject the

medicinal agent. After injection, the handle 372 can be twisted to retract the helical needle into the catheter, thereby removing the needle from the target tissue and freeing the distal end of the catheter from the tissue surface.

The manner of introducing the catheter device is dependent on the approach chosen by the operator and the clinical situation. Entry of the inventive catheter via an arterial entry point is an approach familiar to those skilled in the art. The catheter device is introduced most commonly through the femoral artery. In the absence of adequate arterial access in the groins or due to clinical requirements, the catheter device may be introduced from the brachial artery or the axillary artery in the upper extremities. In some cases, the catheter device may be introduced from the venous circulation, advanced into the right atrium, pushed across the atrial wall and the mitral valve apparatus, and placed in the left ventricular chamber through this approach. In still other applications, it may require the distal end of the catheter device to be placed in other target sites, as one example, the pulmonary circulation.

There are other potential approaches for introducing the inventive device into the body. One approach is to use an introducer as part of a minimally invasive procedure. The catheter is then introduced into the abdomen, chest or elsewhere in the body. A second approach is through a cut-down site or during an operation of any kind. The catheter may also be introduced from the body orifices, such as the mouth, esophagus, trachea, urethra, and the anus, etc. All of the approaches discussed above are familiar to those skilled in the art.

Using the situation where the catheter is introduced into the arterial circulation and the target organ is the left ventricular myocardium as an example,

the catheter device is first advanced in a retrograde fashion into the left ventricular chamber. The operator determines the site(s) on the endocardial surface in the left ventricular chamber for anchoring and attaching the tip of the catheter device. The anchoring step may be bypassed for clinical applications outside of the heart. The general area of attachment for the tip of the catheter device in the left ventricular chamber or at another target tissue is determined before each procedure and is based on the clinical situation and from information obtained from diagnostic studies. Each of the sites for anchoring and attaching the catheter tip during the procedure is localized by fluoroscopy if indicated, with or without the use of contrast dye, echocardiogram, ultrasonogram, or electrocardiogram. Which combination of guiding equipment to be used for the procedure depends on the clinical situation, the skill of the operator, the preference of the operator and the equipment available to the operator. After the exact location of attachment is determined, the operator manipulates the catheter to the designated site and places the tip of the catheter device in direct contact with the endocardial surface at the designated site. As we have described earlier, this process is guided by fluoroscopy if indicated or with other monitoring equipments. This process is also facilitated by using different guiding wires available to the operator. Once the tip of the catheter device is in contact with the endocardial surface at the designated site or the surface of another target site, the operator manipulates the anchoring control means at the proximal end of the catheter device external to the patient. This is connected to and activates a spring-like mechanism or some other anchoring means which emerges from the distal end of the catheter device and which either screws into the endocardial surface or grasps onto the endocardial surface or another target site. This anchors and stabilizes the distal end of the catheter device and prevents it from dislodging from the endocardial surface or another target surface. This is confirmed by fluoroscopy

or other monitoring equipment which shows that the end of the catheter device moves in synchrony with contractions of the left ventricle. This anchoring step may be bypassed for non-cardiac organs or tissues.

The operator now manipulates the needle control means at the proximal end of the catheter device external to the patient. This control means is in continuity to a hollow conduit tubing which runs alongside within the entire length of the catheter device and which is connected to a hypodermic needle at the distal end of the catheter device. This mechanism can be manipulated in increments which is translated in advancement of the needle also in measured increments at the distal end of the catheter device. The needle emerges from the tip of the catheter device penetrates the myocardium or another target tissue to a predetermined depth. The depth of advancement of the needle can be verified by fluoroscopy, echocardiogram other monitoring equipments. The depth of advancement of the hypodermic needle can also be monitored with measurement markings on the proximal handle of the control means which show the movement of the hollow conduit tubing relative to the proximal end of the catheter device.

The needle is hollow and has one or more exit fenestrations or openings. The needle has an inner lumen which is in communication with the exit opening(s) on the needle and is also in communication with a conduit tubing within the catheter device as described. The conduit tubing within the catheter device is connected externally to an injection control means, such as a syringe and reservoir, for the administration of a medicinal agent into the wall of the heart or another target tissue. The volume of medicinal agents in the syringe, conduit tubing and hypodermic needle is calibrated prior to or during the procedure. The process is repeated within the left ventricular chamber or at another target site for as many

times as needed and after the whole procedure is completed, the catheter device is removed from the patient.

Although the above description contains many specifics of that embodiment, these should not be construed as limiting the scope of the invention. For example, the number of exit fenestration or openings and the locations of these exit openings on the needles may vary depending on the manner by which the medicinal agent needs to be distributed; the configuration of the exit openings on the needle may be variable depending on the clinical situation; the configurations of the needle may vary; the means by which the tip of the catheter device is stabilized on the endocardial surface may be variable; the catheter device may be of a different configuration to deliver a novel medicinal agent to the coronary circulation, other parts of the heart, the lung organ or the pulmonary circulation., etc. Those of skill in the art will be able to make these and many other modifications to the catheter device of the invention. The scope of this invention is determined solely by the following claims.

CLAIMS

1. A device for administering a medical agent directly to a bodily organ comprising:

a hollow catheter having a proximal end and a distal end;

anchoring means for securing the distal end of the catheter to an organ surface, the anchoring means being movable between a retracted position in which the anchoring means is within the catheter and an attachment position in which at least a portion of the anchoring means protrudes from the distal end of the catheter for securement to an organ surface;

anchor control means for moving the anchoring means between the retracted position and the attachment position;

medical agent delivery means within the catheter for delivering a medical agent to a bodily organ.

2. The device of claim 1 wherein the anchor control means is located at the proximal end of the catheter.

3. The device of claim 1 wherein the anchoring means comprises a helical coil having a sharpened end for penetration of an organ surface, the anchoring means being reciprocally movable from the retracted position to the attachment position by twisting to embed the sharpened end in the organ.

4. The device of claim 3 wherein the anchor control means comprises a grip connected to the helical coil for rotatably twisting the helical coil in a first direction to advance the coil from the retracted position to the attachment position and for rotatably twisting the helical coil in a second direction opposite to that of the first direction to retract the helical coil from the attachment position to the retracted position.

5. The device of claim 3 wherein the catheter has pitched internal threads which engage the helical coil such that the helical coil is advanced or retracted as it is twisted.

6. The device of claim 1 wherein the delivery means and anchoring means jointly comprise a hollow bore hypodermic needle in the form of a helical coil having a sharpened end for penetration of an organ surface which is reciprocally movable from the retracted position to the attachment position by twisting to embed or disembed the sharpened end in or from the organ.

7. A device for the injection of a medicinal agent into a bodily organ comprising:

a catheter having a proximal end, a distal end, at least one continuous conduit traversing the catheter from the proximal end to the distal end and having openings at the proximal and distal ends;

a hollow bore needle having an exit opening and an entrance opening and being movable between a retracted position in which the hollow bore needle is within a conduit and an injecting position in which the exit opening of the hollow

bore needle protrudes from the opening of the conduit at the distal end of the catheter;

needle control means at the proximal end of the catheter for moving the hollow bore needle between the retracted position and the injecting position;

injection control means for controlling the introduction of liquid medical agent into, through and out of the hollow bore needle;

anchoring means for securing the distal end of the catheter to an organ surface, the anchoring means being movable between a retracted position in which the anchoring means is within a conduit and an attachment position in which at least a portion of the anchoring means protrudes from the conduit opening at the distal end of the conduit for securement to an organ surface; and

an anchor control means for moving the anchoring means between the retracted position and the attachment position.

8. The device of claim 7, wherein the anchoring means comprises:

a helical coil having a sharpened end at the distal end of the catheter for penetration of an organ surface, the anchoring means being reciprocally movable from the retracted position to the attachment position by twisting to embed the sharpened end in the organ.

9. The device of claim 8, wherein in the anchor control means comprises:

a grip connected to the helical coil for rotatably twisting the helical coil in a first direction to advance the coil from the retracted position to the attachment position and for rotatably twisting the helical coil in a second direction opposite to that of the first direction to move the helical coil from the attachment position to the retracted position.

10. The device of claim 8 wherein the catheter has pitched internal threads which engage the helical coil such that the helical coil is advanced or retracted as it is twisted.

11. The device of claim 7, further comprising guide means for guiding the catheter through bodily orifices or vessels to a specific site on an organ

12. The device of claim 11, wherein the guide means comprises stiffening means for bracing the catheter sufficiently to allow the catheter to be snaked through bodily vessels to a specific site on an organ.

13. The device of claim 8 further comprising means for guiding the catheter through bodily orifices or vessels to the specific site.

14. The device of claim 13, wherein the guide means comprises stiffening means for bracing the catheter sufficiently to allow the catheter to be snaked through bodily vessels to a specific site on an organ.

15. The device of claim 11 wherein the guide means is a wire.

16. The device of claim 13 wherein the guide means is a wire.

17. The device of claim 7 wherein the catheter has at least two conduits and each of the hollow bore needle and anchoring means are housed in different conduits.

18. The device of claim 11, having at least two conduits and wherein the guide means is housed in a conduit different from the hollow bore needle and the anchoring means.

19. The device of claim 11 wherein the catheter has at least three conduits and each of the hollow bore needle, the anchoring means and the guide means are housed in different conduits.

20. The device of claim 7, wherein the injection control means comprises a syringe in communication with the hollow bore needle.

21. The device of claim 7, wherein at least one of the conduits has at the opening at the distal end a closing means for preventing entry of foreign bodies and fluid into he conduit.

22. The device of claim 21, wherein the closing means is liquid impermeable, is formed from an elastic deformable material and is penetrable by the needle or anchoring means.

23. The device of claim 7 wherein the proximal end of the device is wider than the distal end and the conduit opening at the proximal end are spaced as far apart as possible.

24. The device of claim 7 composed of a material that is opaque to fluoroscopy.

25. The device of claim 7, wherein the anchoring means comprises three or more prongs which pierce or grasp a surface of the specific site.

26. A method of injecting a liquid medical agent into a bodily organ using the device of claim 1 comprising:

a) loading the medical agent delivery means with liquid medical agent;

b) Introducing the distal end of the catheter into an orifice of the body;

c) positioning the distal end of the catheter adjacent an organ of the body to be injected;

d) moving the anchoring means to the attachment position and attaching the anchoring means to the organ to be injected;

e) introducing the medical agent to the organ with the medical agent delivery means.

27. The method of claim 26 wherein the anchoring means comprises a helical coil having a sharpened end for penetration of an organ surface, the anchoring means being reciprocally movable from the retracted position to the attachment position by twisting to embed the sharpened end in the organ.

28. A method of injecting a liquid medical agent into a bodily organ using the device of claim 7 comprising:

a) loading the medical agent delivery means with liquid medical agent;

b) introducing the distal end of the catheter into an orifice of the body;

c) positioning the distal end of the catheter adjacent an organ of the body to be injected;

d) moving the anchoring means to the attachment position and attaching the anchoring means to the organ to be injected;

e) moving the needle into the injecting position wherein it penetrates into the organ to a sufficient depth for injection;

f) introducing the medical agent through and out of the needle and into the organ with the injection control means;

29. The method of claim 28 wherein the device further comprises guide means for guiding the catheter through bodily orifices or vessels to a specific site on an organ.

30. The method of claim 28 wherein the injection control means comprises a syringe in communication with the hypodermic needle.

31. The method of claim 30 wherein the organ is the heart.

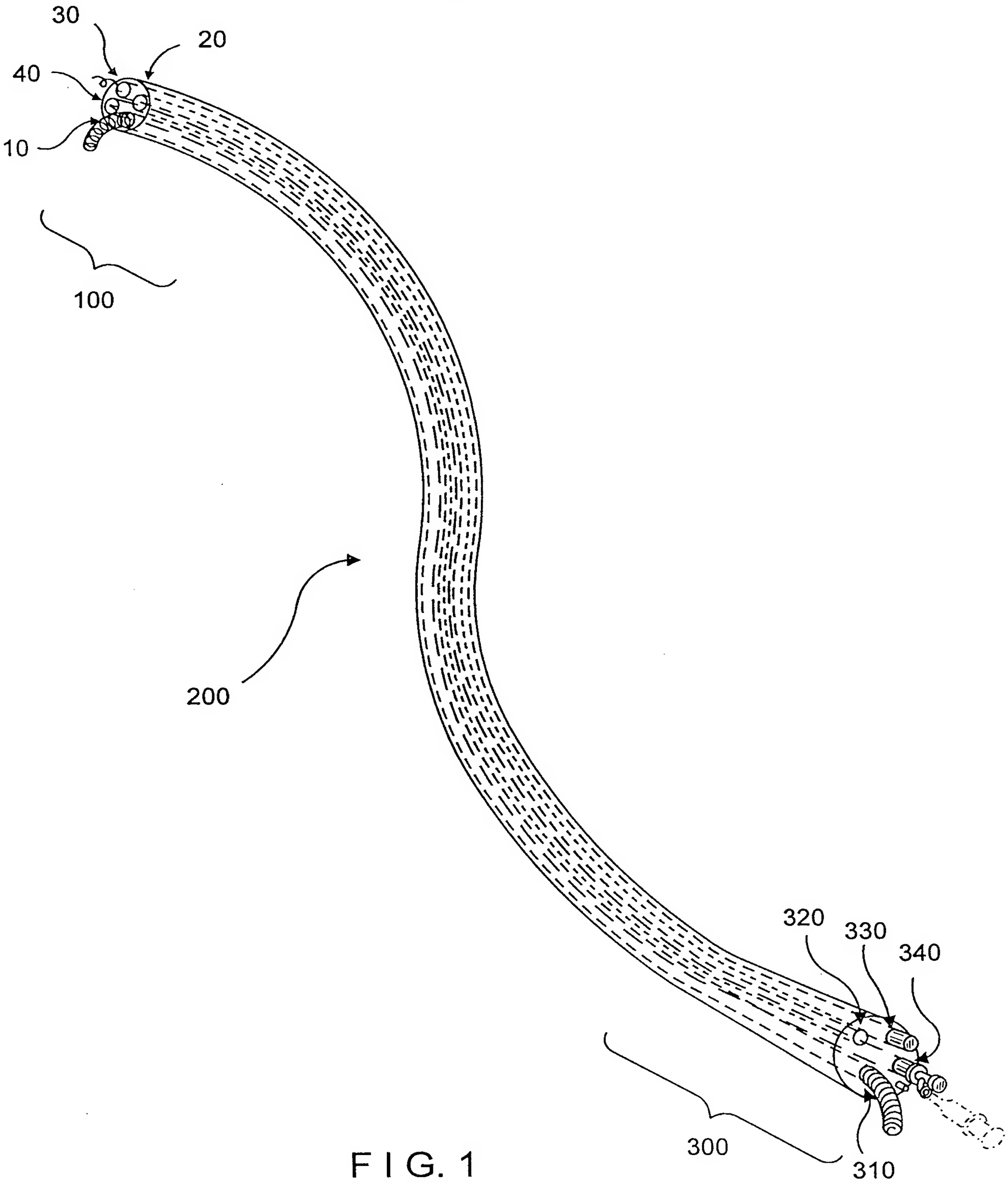

FIG. 1

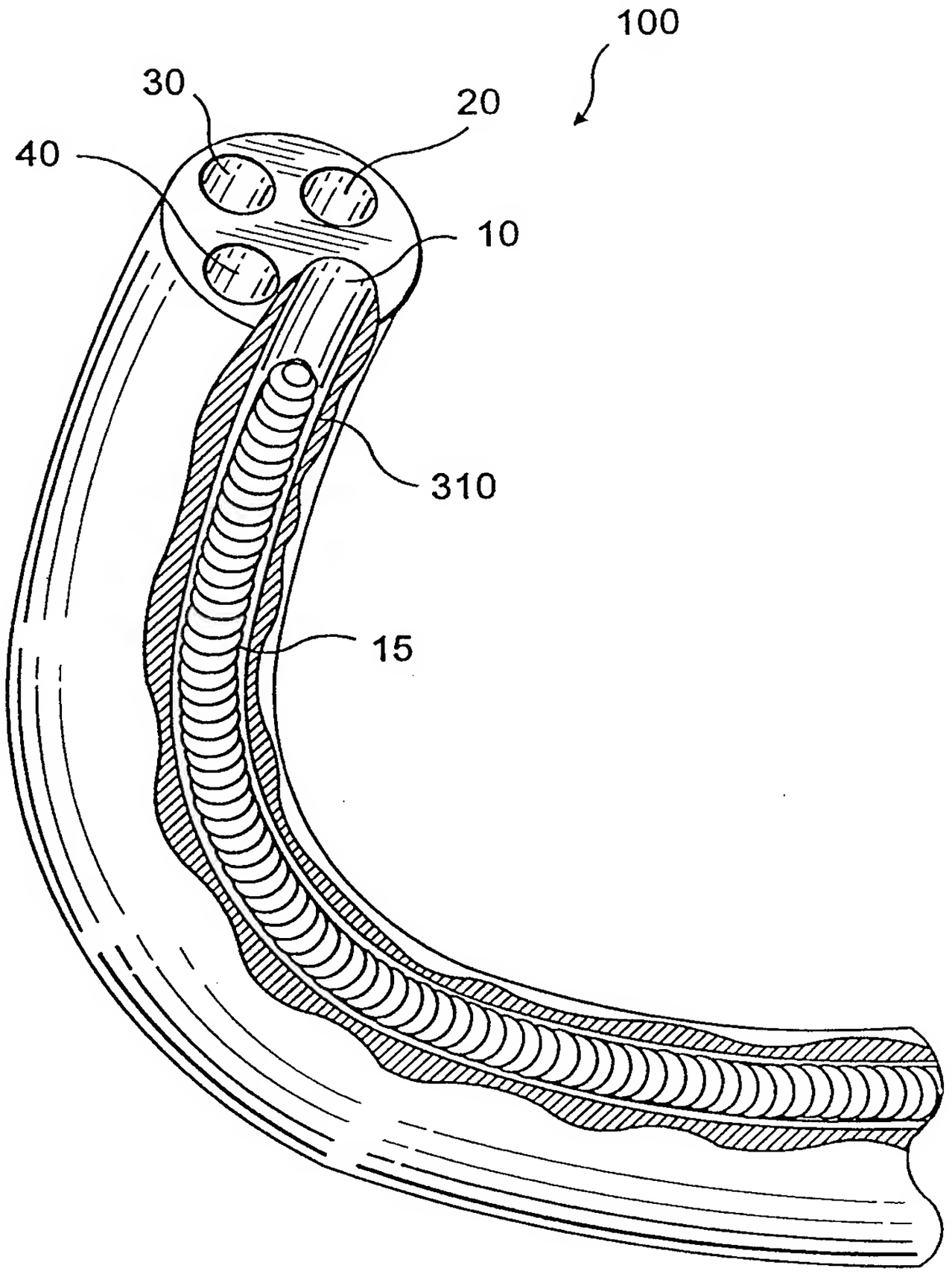

FIG. 2

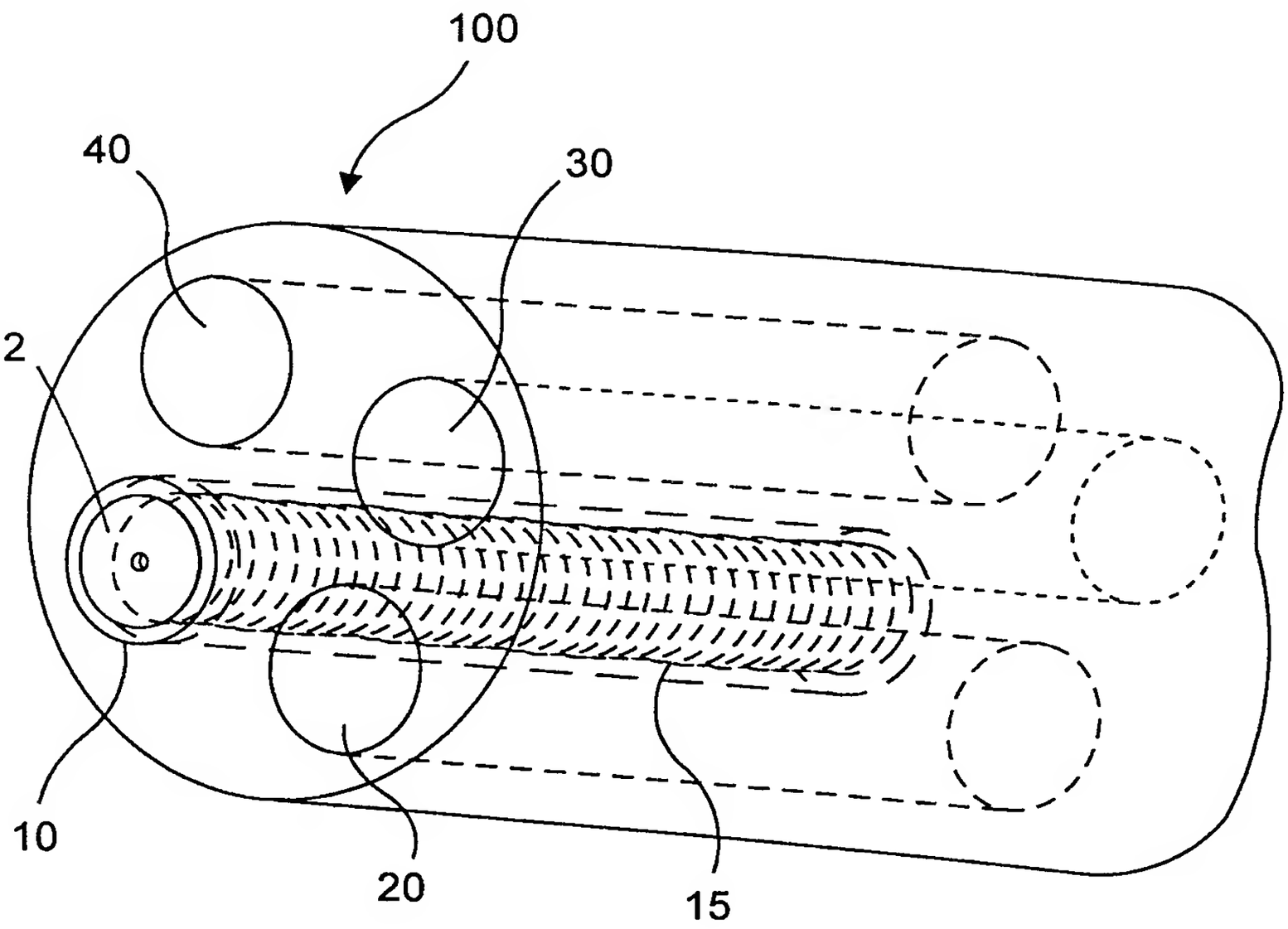

FIG. 3

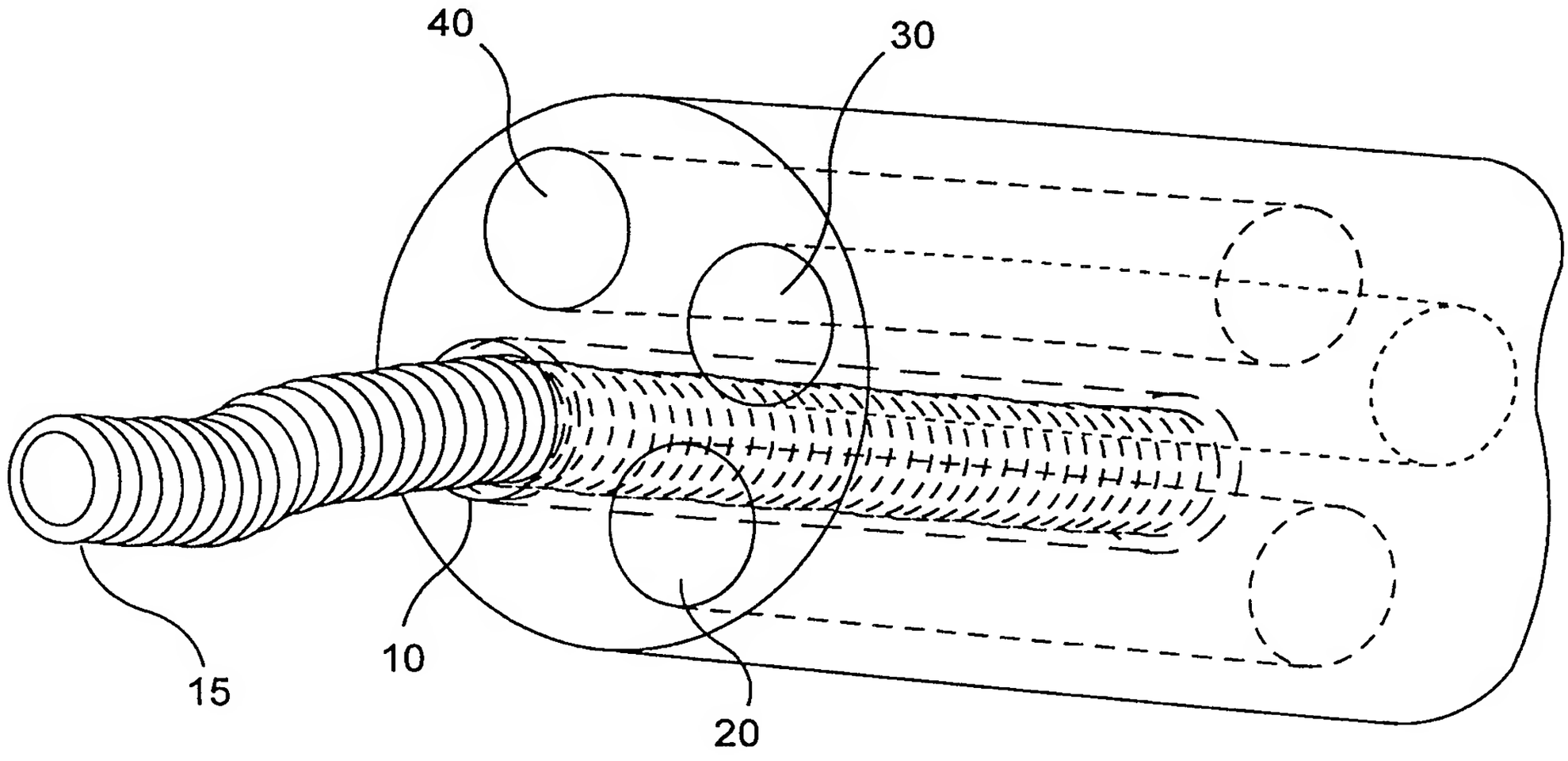

FIG. 4

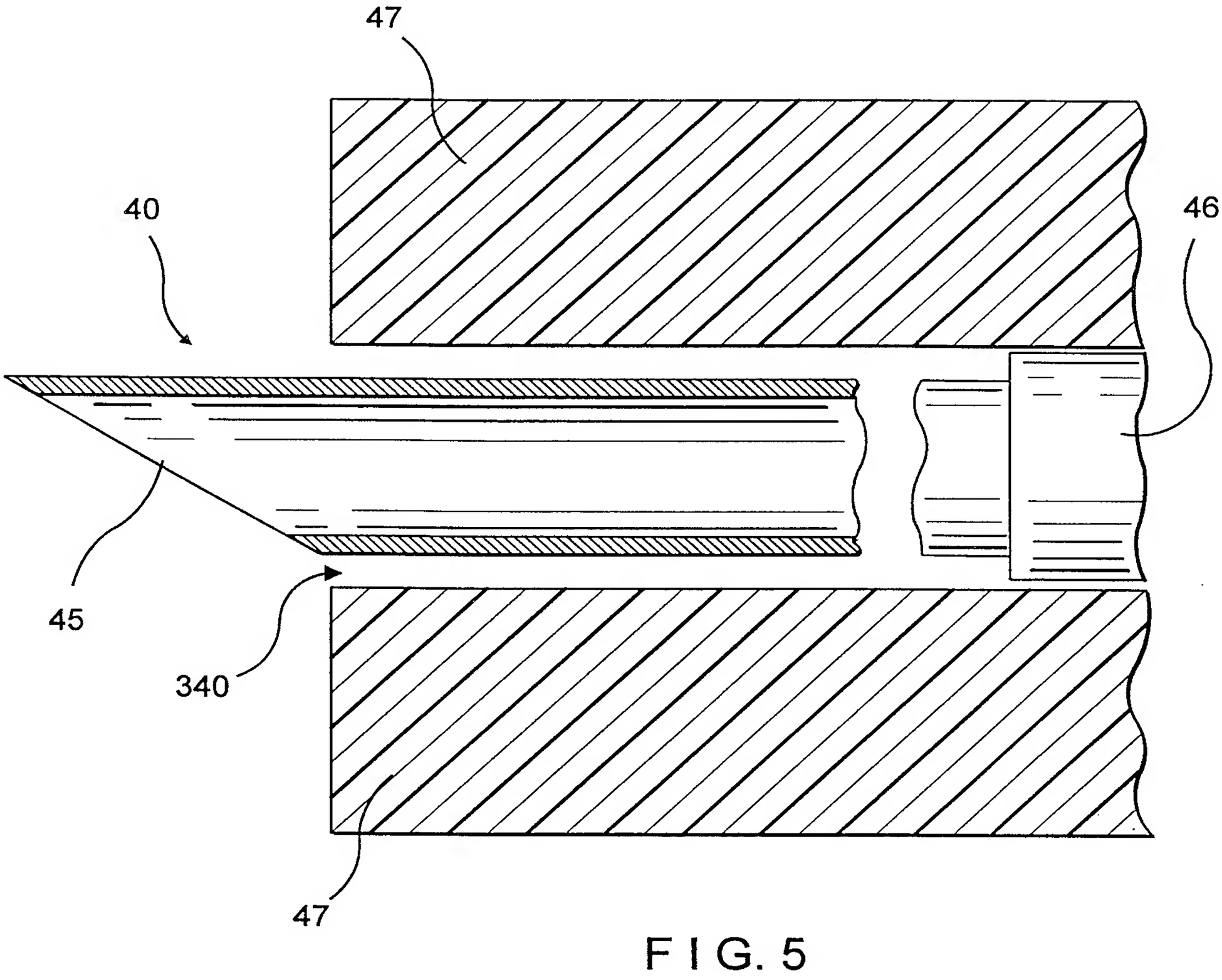

FIG. 5

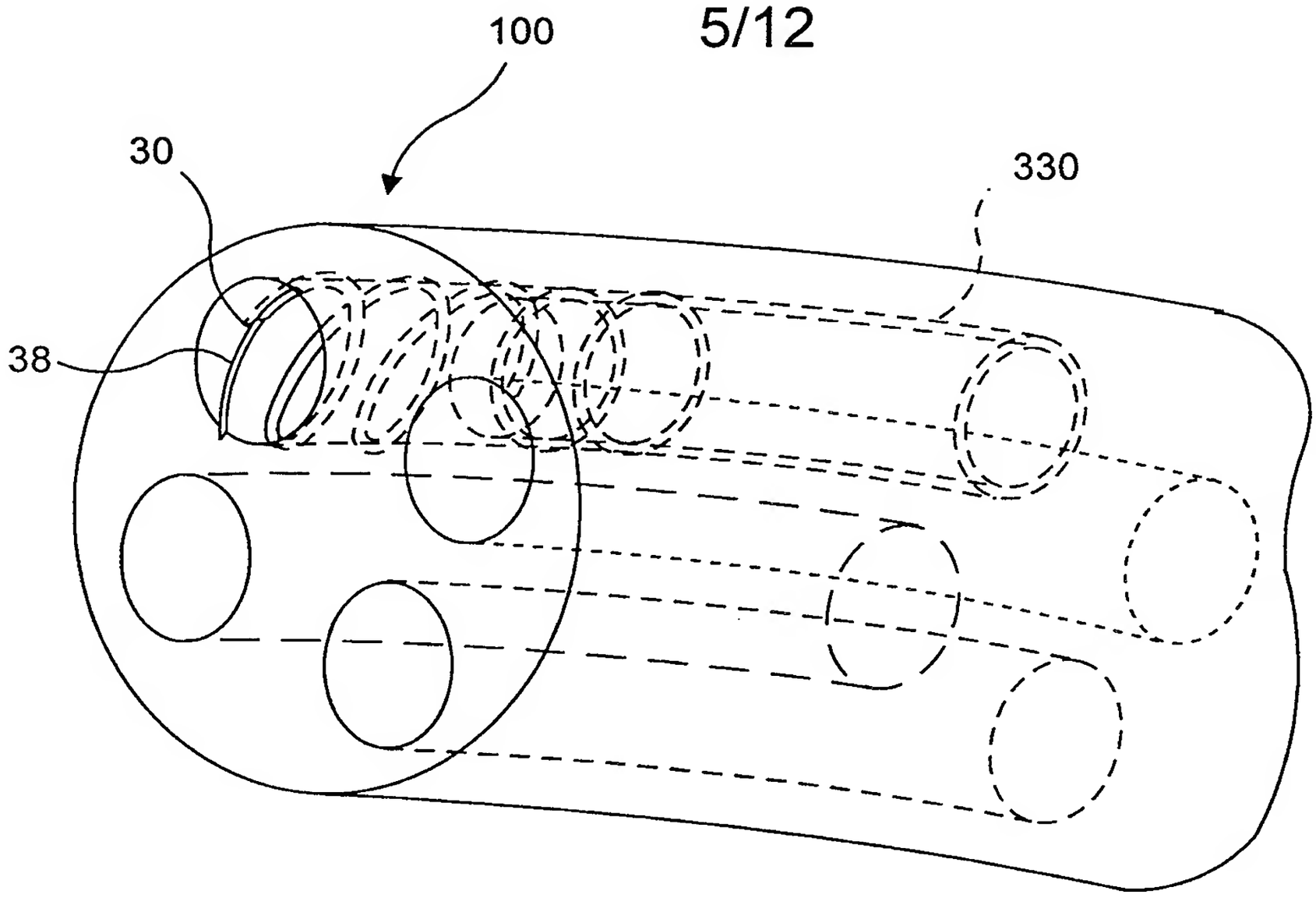

FIG. 6

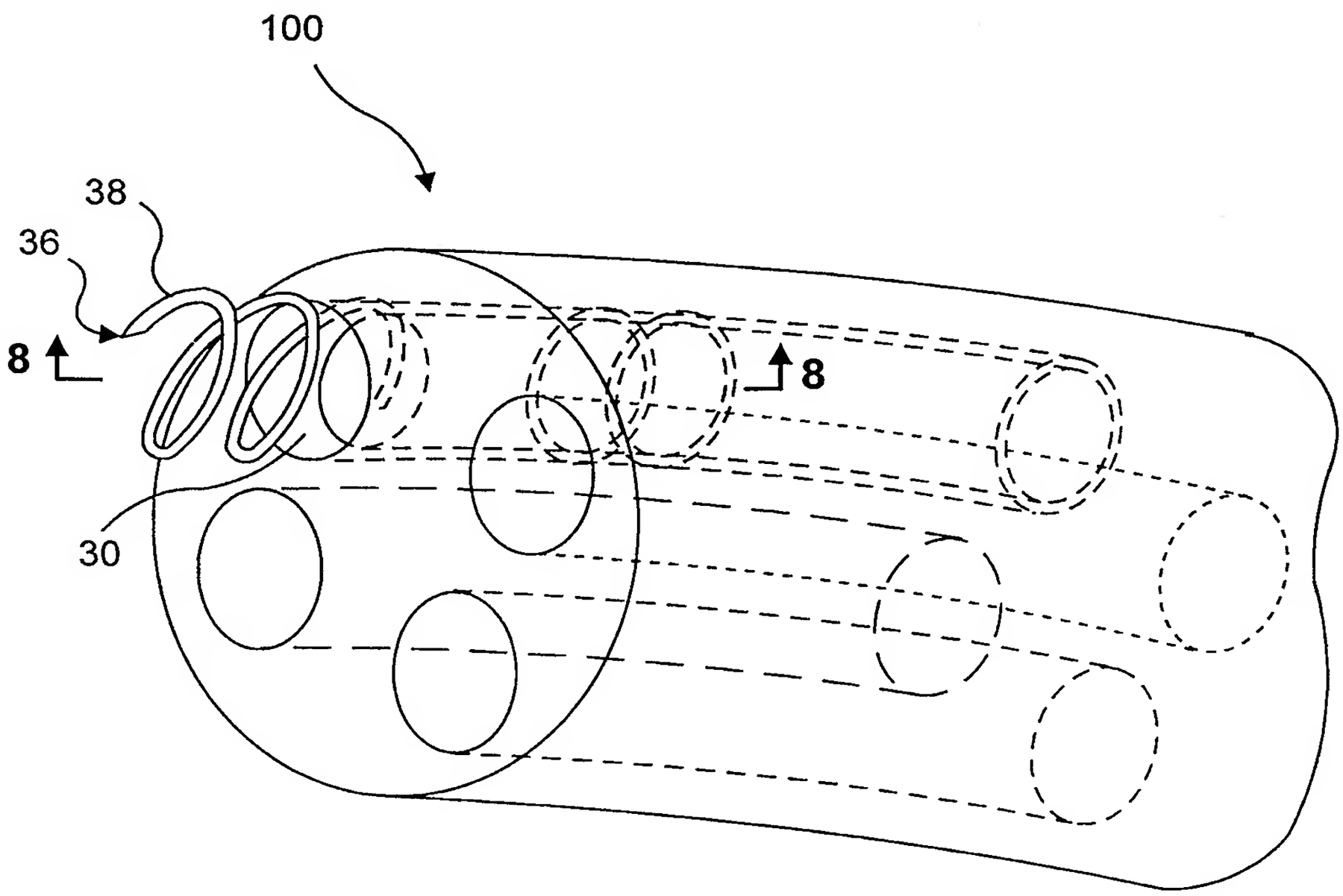

FIG. 7

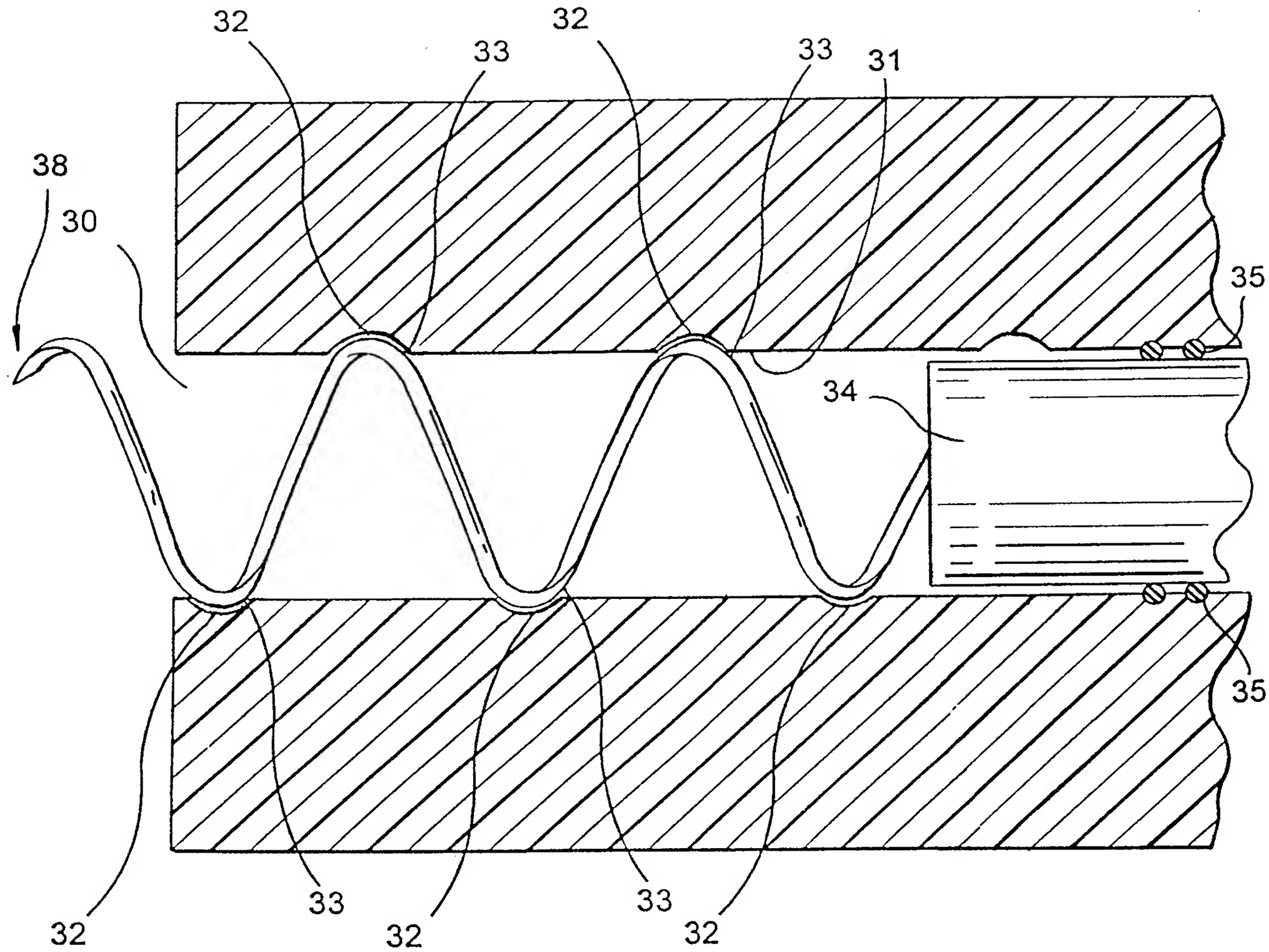

FIG. 8

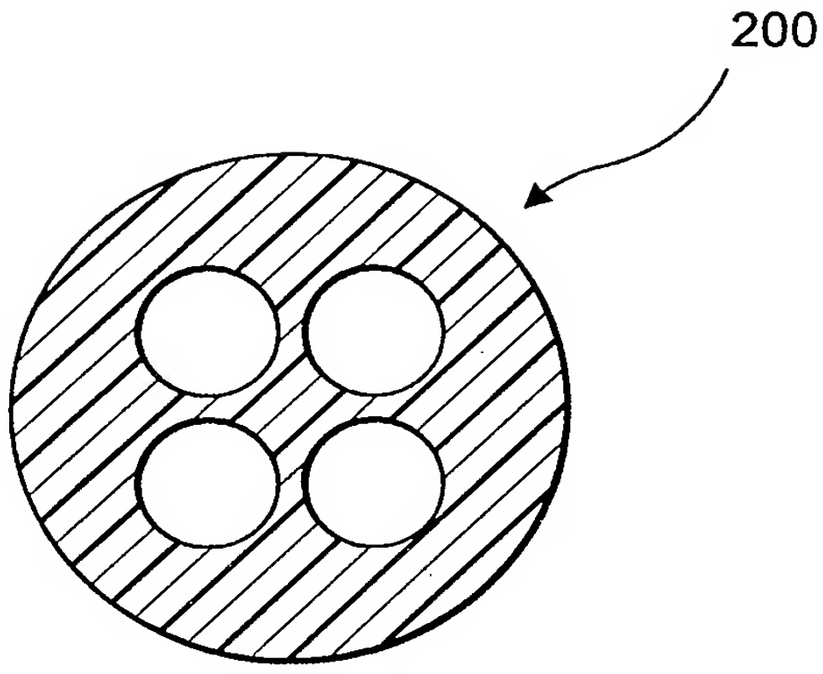

FIG. 9

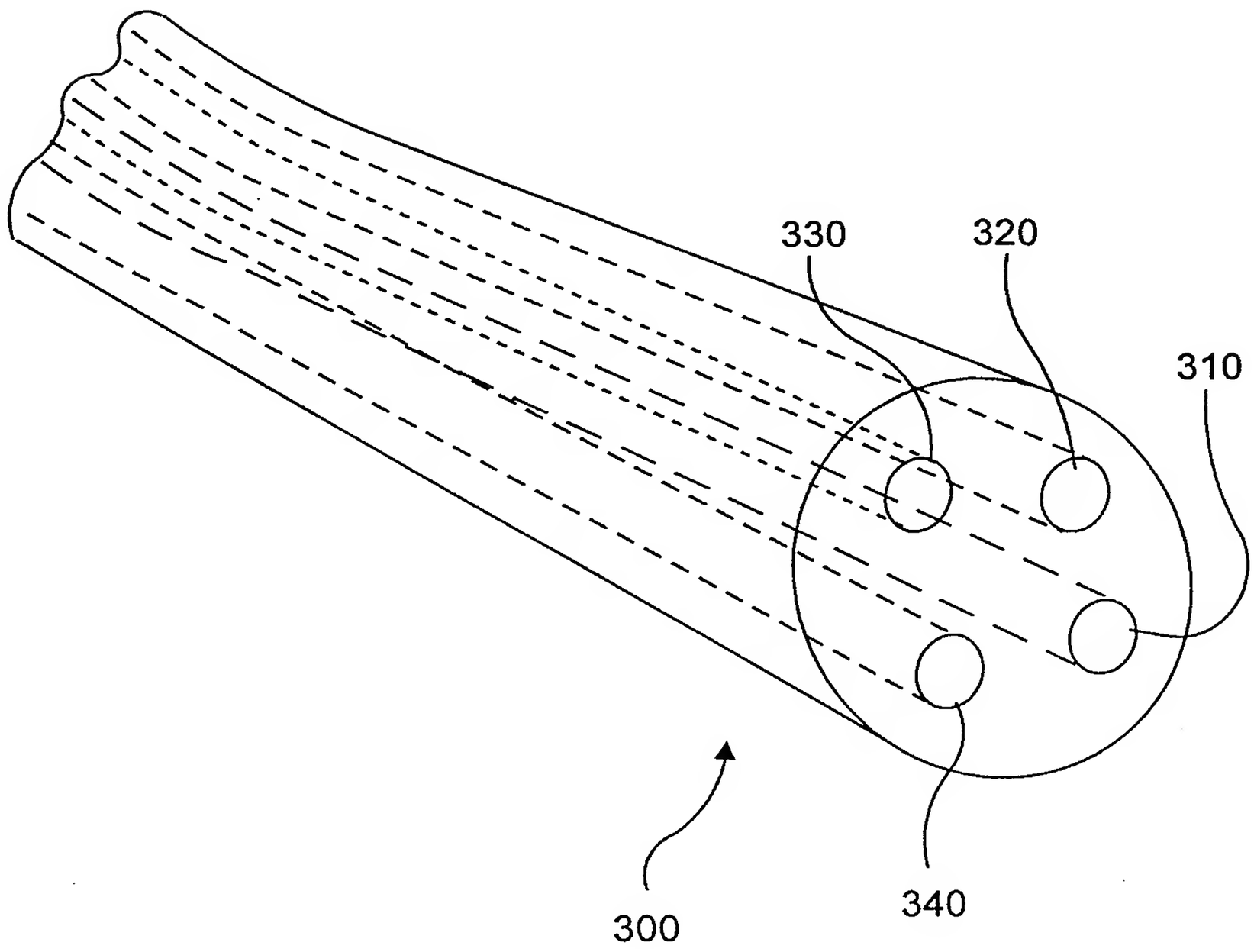

FIG. 10

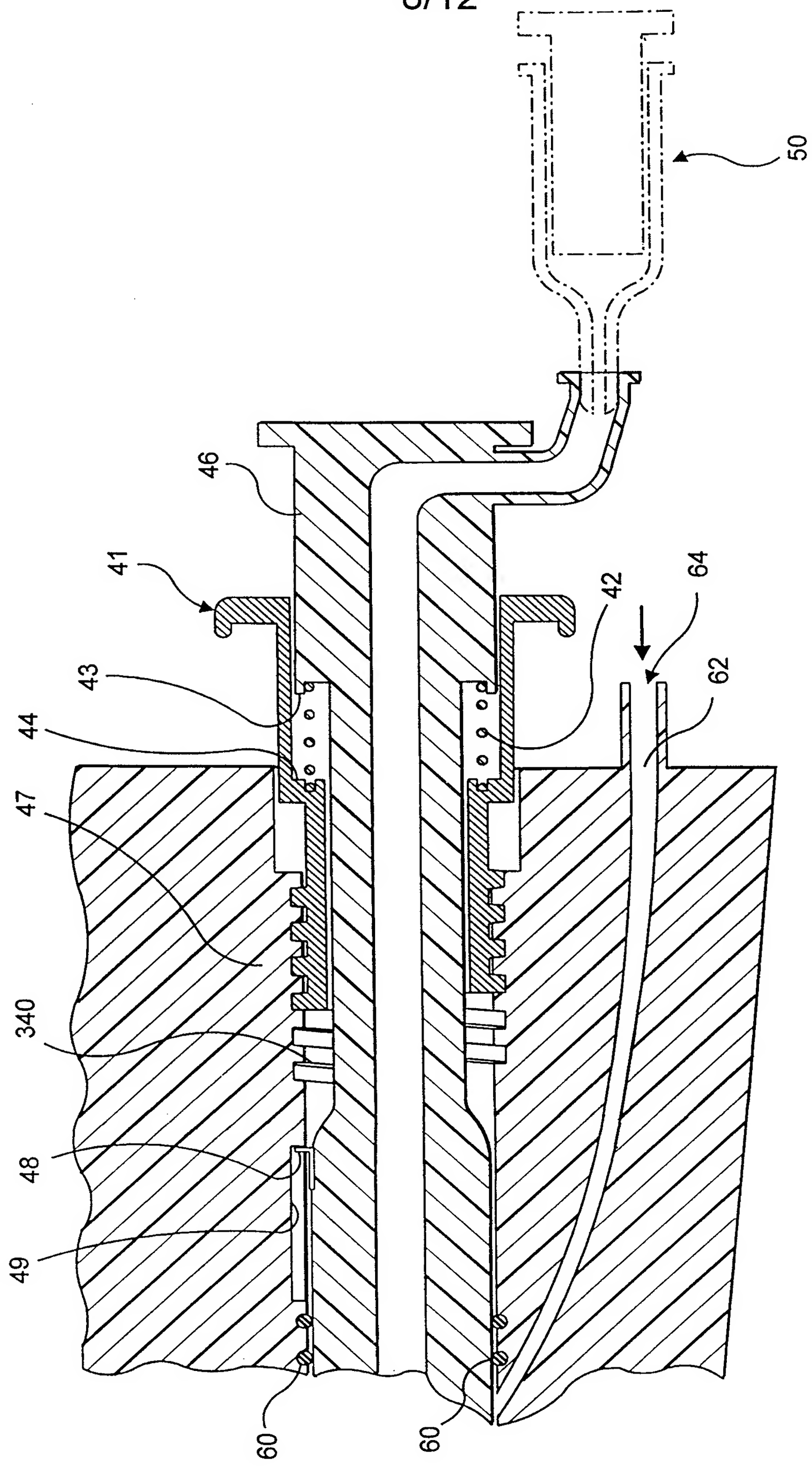

FIG. 11

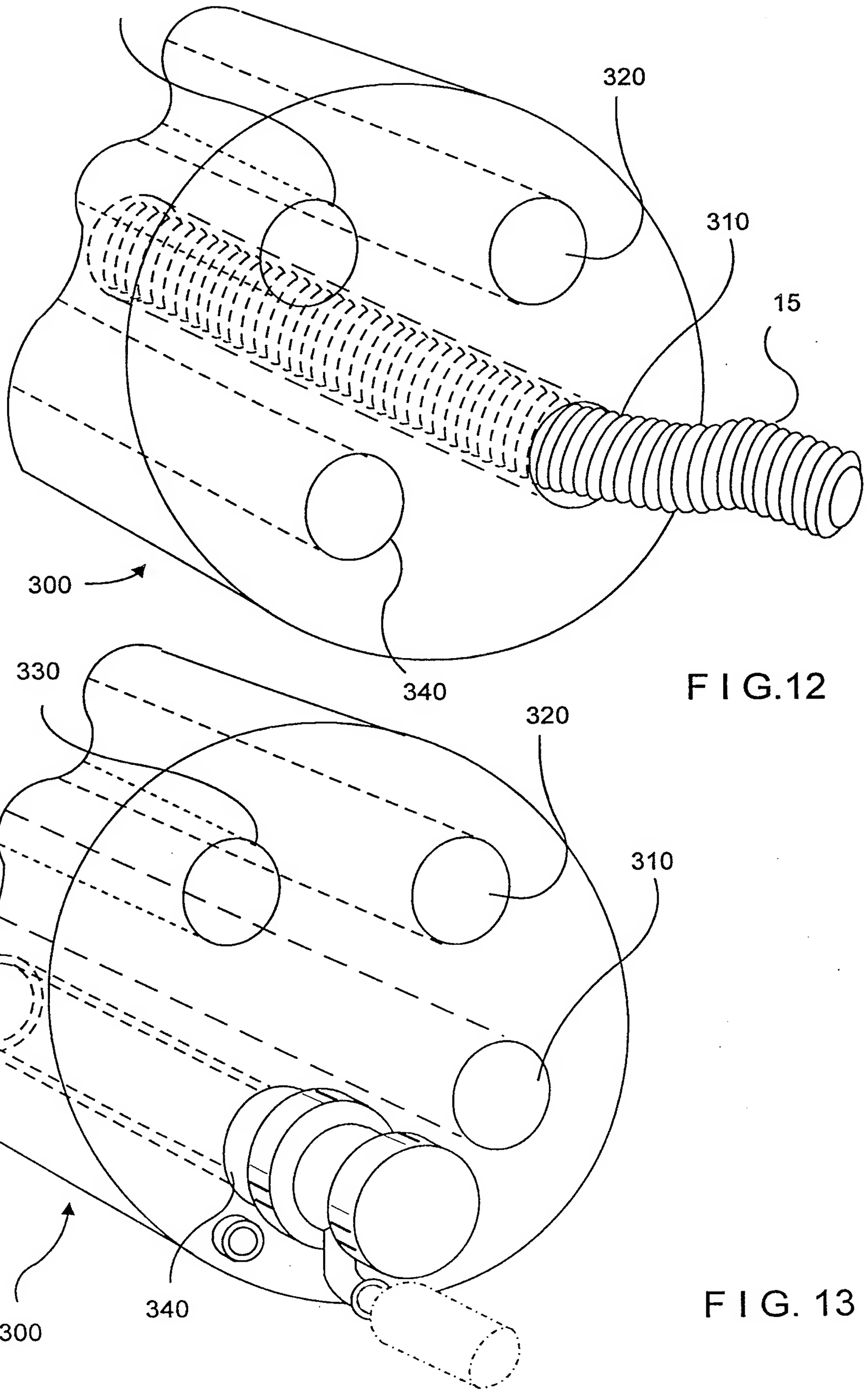

FIG.12

FIG. 13

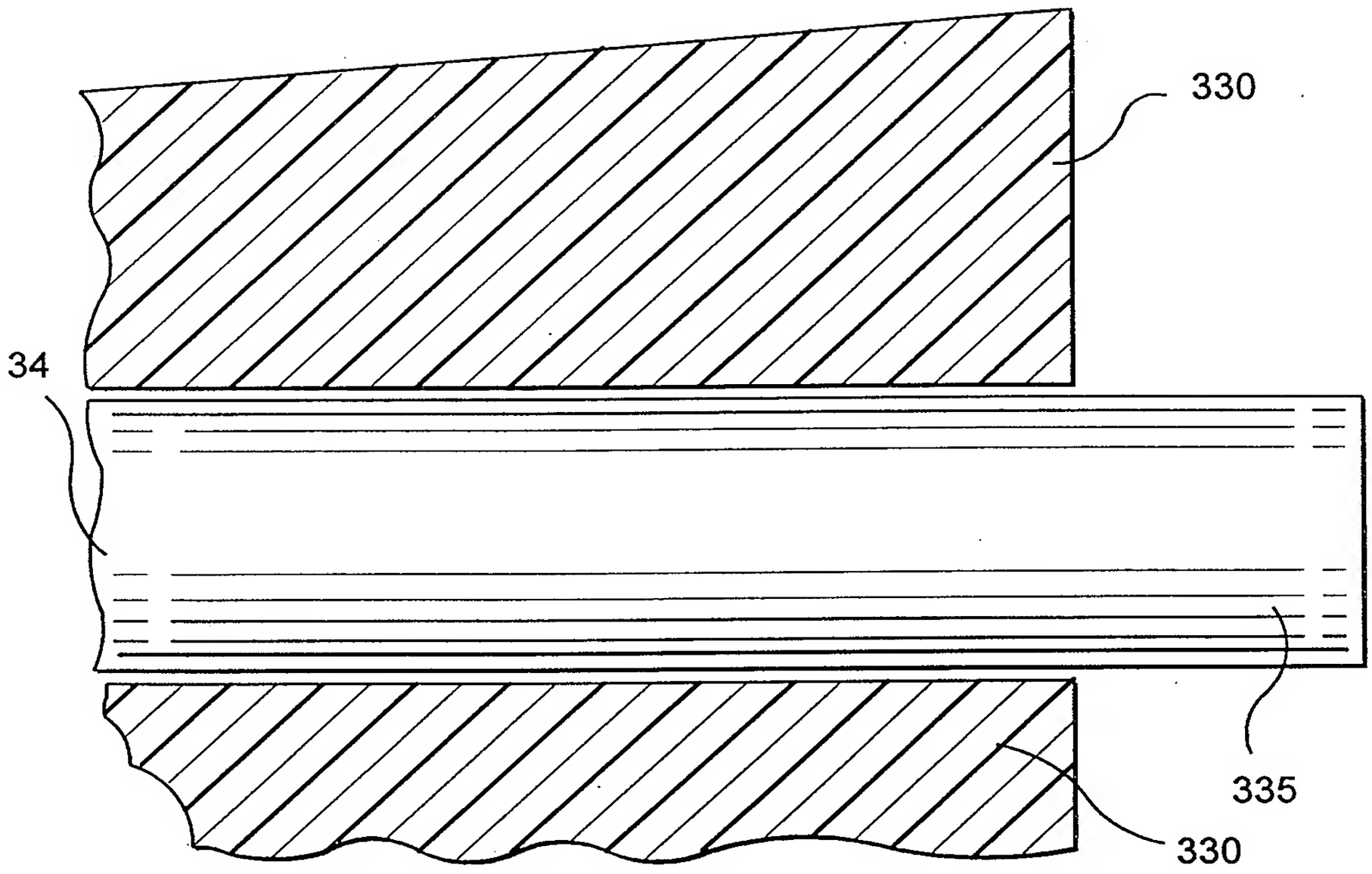

FIG. 14

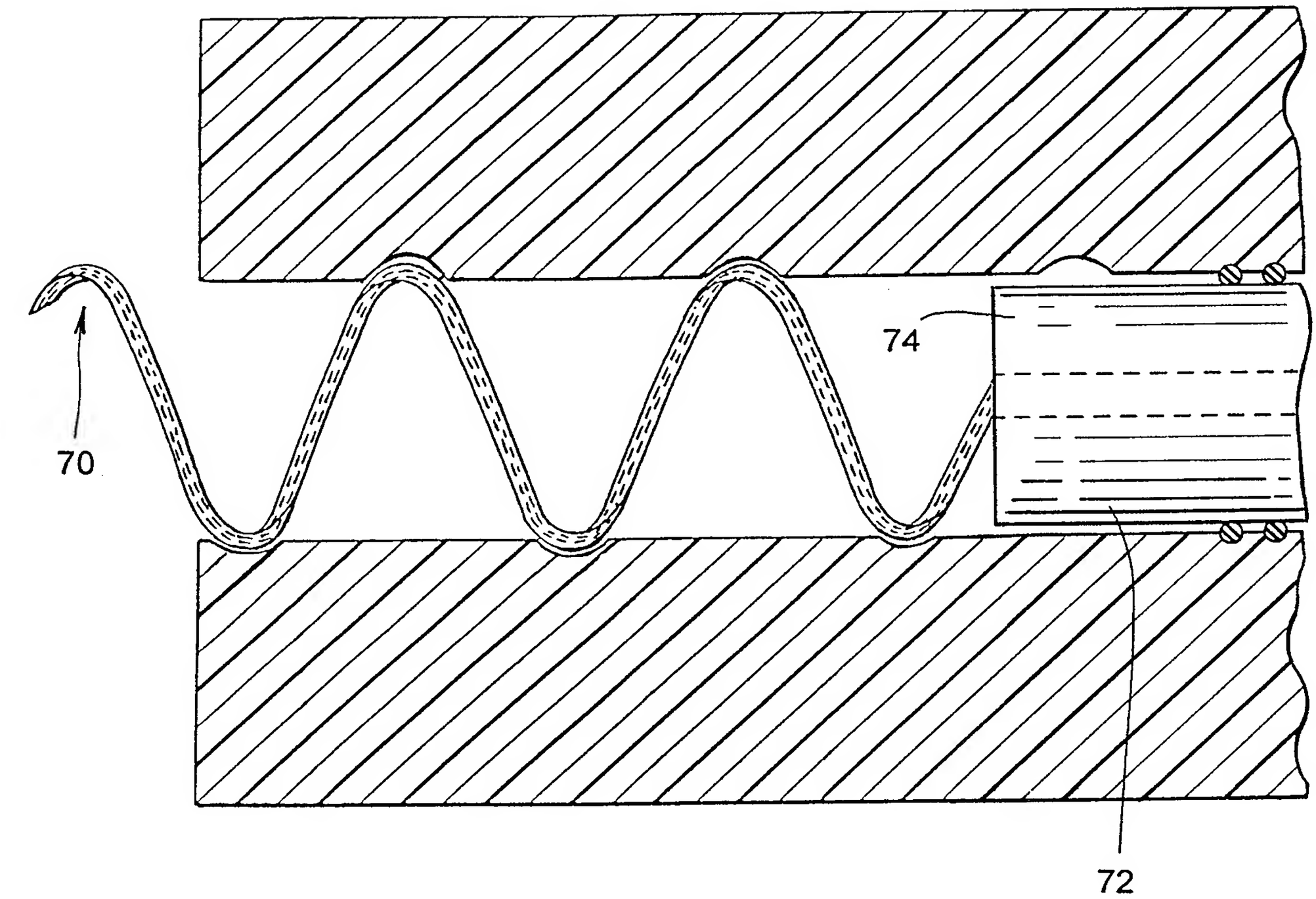

FIG. 15

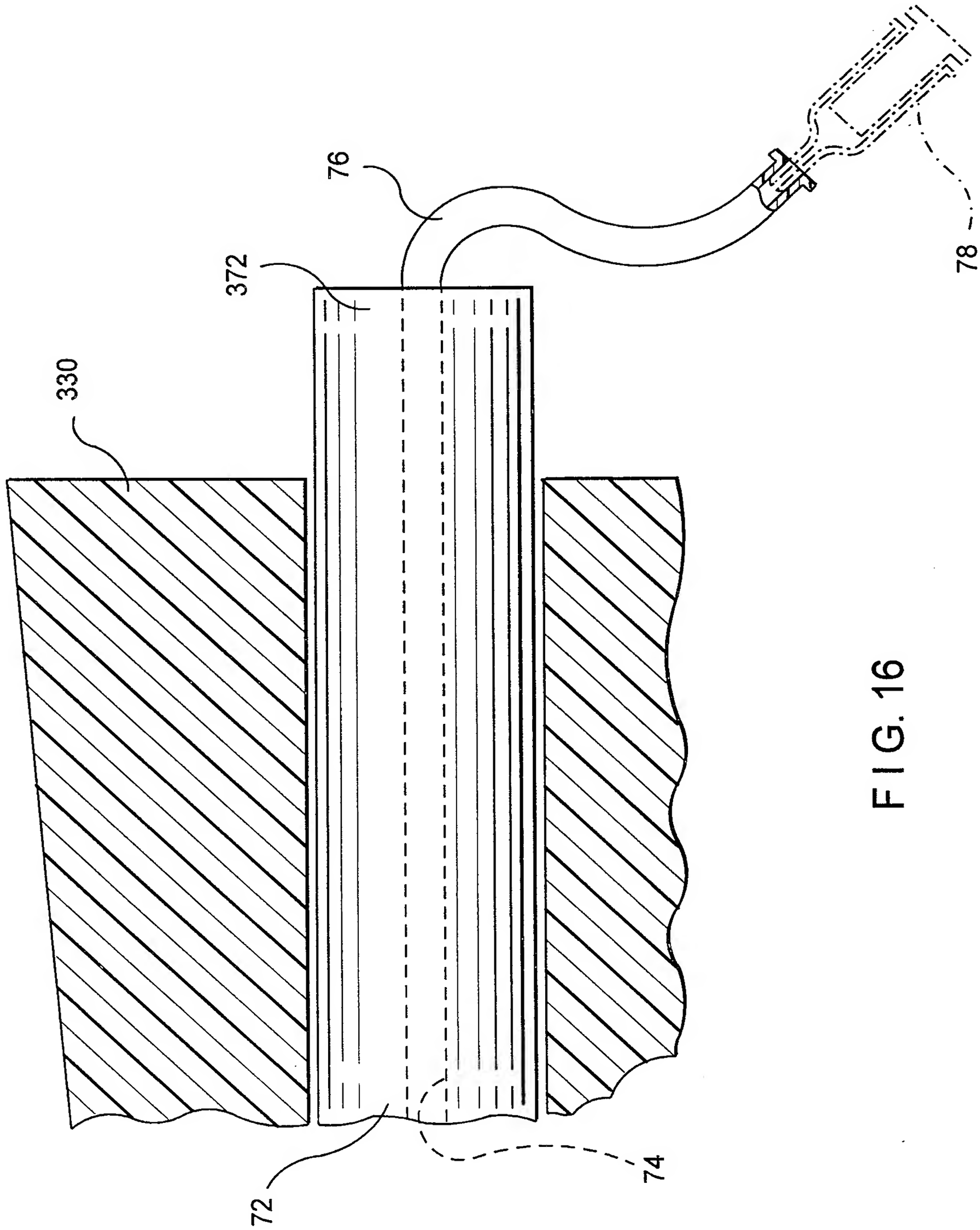

FIG. 16

INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 99/08681

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M25/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 222 380 A (TERAYAMA TOSHIKI) 16 September 1980 (1980-09-16) column 4, line 11 -column 5, line 61; figures	1,2,7,20
A	US 5 256 146 A (ENSMINGER WILLIAM D ET AL) 26 October 1993 (1993-10-26) column 3, line 14 -column 4, line 33; figures	1-4,6-9, 11-16
A	EP 0 564 321 A (CELSA L G SA) 6 October 1993 (1993-10-06) column 7, line 37 - line 46; figure 11	1-3,6-8
A	US 5 431 649 A (HOEY MICHAEL F ET AL) 11 July 1995 (1995-07-11) abstract; figures	1,3,6-8

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 September 1999	05/10/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Kousouretas, I

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 99/08681

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 24373 A (ANGIOTRAX INC) 11 June 1998 (1998-06-11) page 32, line 25 -page 33, line 13; figure 17A	1-4,7-9
A	US 5 769 821 A (YOUNG PAULINE R ET AL) 23 June 1998 (1998-06-23) abstract; figures	1,3,7,9

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/08681

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 26-31
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT- Method for treatment of the human or animal body by surgery

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter nal Application No
PCT/US 99/08681

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